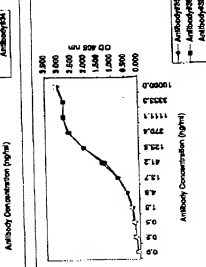
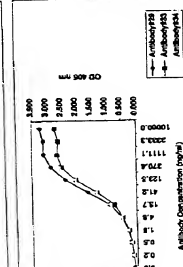
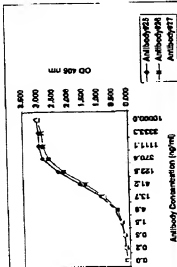
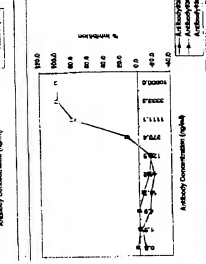
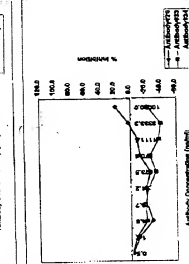
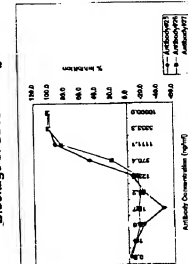


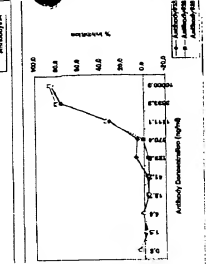
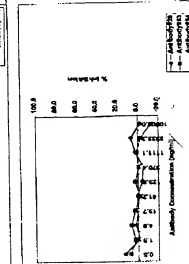
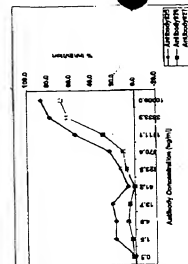
# Binding of antibodies to CTLA-4



## Blockage of CD86 binding



## Blockage of CD80 binding



# Anti-CTLA4 Abs #25, #26, and #29 defined three distinct epitopes on CTLA4

CTLA4 point mutant	Antibody #25
Mock	0.165
WT	1.17
T67	0.935
Q82	1.1
R85	0.96
D63	0.986
R38	0.52
S64	1.07
I65	1.19
L61	1.14
T45	0.948
E46	0.811
D62	0.965
CTLA4-Ig	0.966
DME	0.14

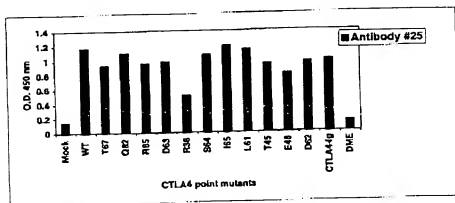


Fig.  
2A

CTLA4 point mutant	Antibody #26
Mock	0.174
WT	1.16
T67	0.944
Q82	1.07
R85	0.976
D63	0.970
R38	0.836
S64	1.1
I65	1.17
L61	1.19
T45	0.948
E46	0.16
D62	0.874
CTLA4-Ig	1.1
DME	0.163

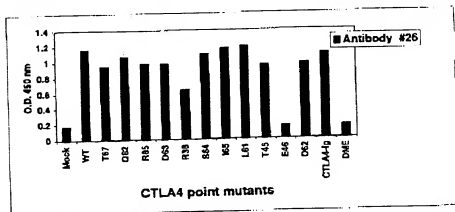


Fig.  
2B

CTLA4 point mutant	Antibody #29
Mock	0.094
WT	0.82
T67	0.635
Q82	0.794
R85	0.956
D63	0.713
R38	0.364
S64	0.763
I65	0.801
L61	0.819
T45	0.885
E46	0.609
D62	0.873
CTLA4-Ig	0.857
DME	0.091

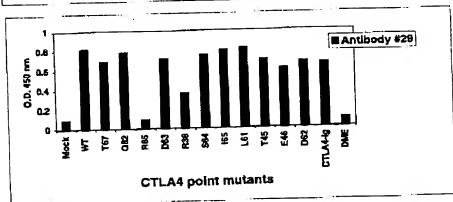


Fig.  
2C

Fig 3A Proliferation

	media	Ab #25	Ab #26	Ab#27	Ab#29	Ab#33	Ab#34	Ab#35	Ab#36	Ab #38
Donor 1	54871	16569	33926	49492	234	928	45524	56203	72358	50865
Donor 2	102159	32764.3	58736.2	79098.2	1891.3	5427.4	78391.9	91920.2	116454.8	88937.3

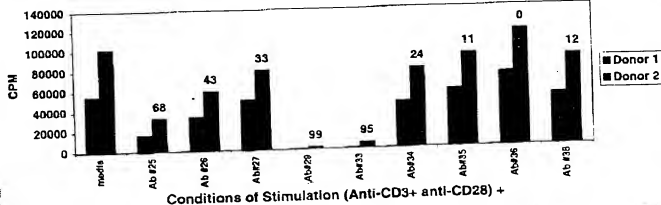


Fig 3B IL-2 Production

	media	Ab #25	Ab #26	Ab#27	Ab#29	Ab#33	Ab#34	Ab#35	Ab#36	Ab #38
IL-2(pg/ml)	2125.3	330.2	182.5	231.7	60.8	462.3	573.7	305.7	617.7	672.1

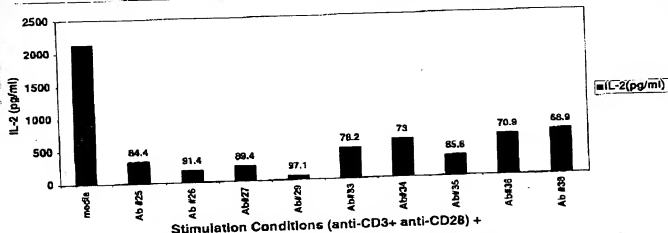


Fig. 4A Proliferation

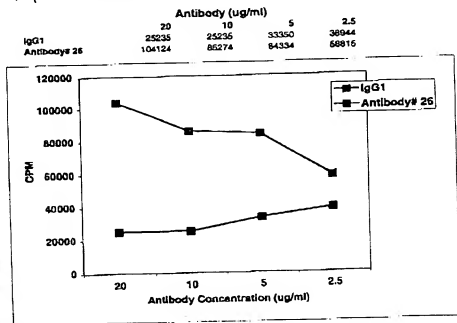
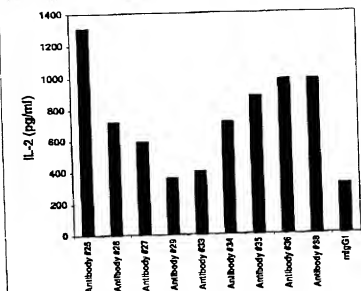


Fig. 4B IL-2 Production

Antibody #25	1310
Antibody #26	720
Antibody #27	594
Antibody #29	358
Antibody #33	480
Antibody #34	715
Antibody #35	875
Antibody #36	982
Antibody #38	982
mIgG1	317



1303032269

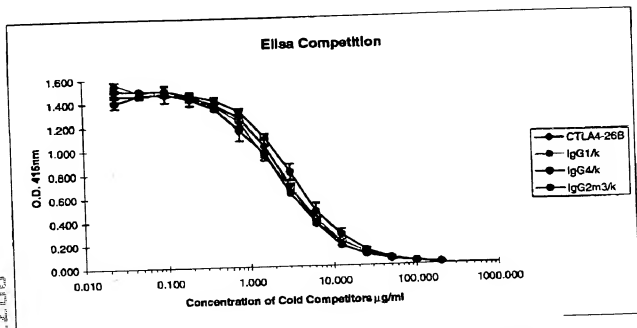


Figure 5

**FACS Competition Using FITC-Labeled CTLA4-26B with Cold CTLA4-26B and Humanized IgG1/ $\kappa$**

Name	Cell Line	Primary Ab	Competitor
052199.001	CHO.CTLA4	FITC-CTLA4-26B 125 ng	Cold CTLA4-26B 2000 ng
052199.002			1000 ng
052199.003			500 ng
052199.004			250 ng
052199.005			100 ng
			IgG1/ $\kappa$
052199.006	CHO.B7.1	none	2000 ng
052199.007			1000 ng
052199.008			500 ng
052199.009			250 ng
052199.010			100 ng
052199.016		125 ng	none
052199.017		125 ng	none
052199.018		none	none
052199.019		none	none

Fig  
6A

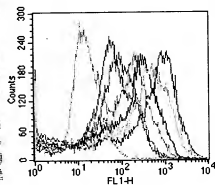


Fig  
6B

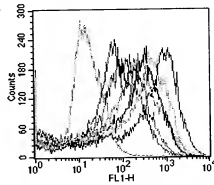
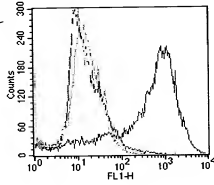


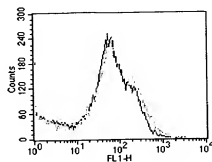
Fig  
6C



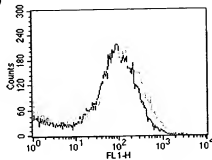
Key	Name	Parameter	Gate
—	052199.016	FL1-H	No Gate
—	052199.017	FL1-H	No Gate
—	052199.001	FL1-H	No Gate
—	052199.002	FL1-H	No Gate
—	052199.003	FL1-H	No Gate
—	052199.004	FL1-H	No Gate
—	052199.005	FL1-H	No Gate

Key	Name	Parameter	Gate
—	052199.016	FL1-H	No Gate
—	052199.017	FL1-H	No Gate
—	052199.006	FL1-H	No Gate
—	052199.007	FL1-H	No Gate
—	052199.008	FL1-H	No Gate
—	052199.009	FL1-H	No Gate
—	052199.010	FL1-H	No Gate

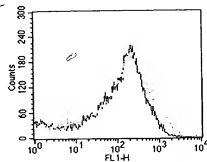
Key	Name	Parameter	Gate
—	052199.016	FL1-H	No Gate
—	052199.017	FL1-H	No Gate
—	052199.018	FL1-H	No Gate
—	052199.019	FL1-H	No Gate

Fig.  
7A

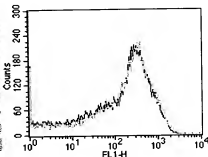
Key	Name	Parameter	Gate
—	052199.001	FL1-H	No Gate
---	052199.006	FL1-H	No Gate

Fig  
7B

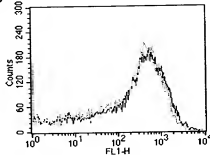
Key	Name	Parameter	Gate
—	052199.002	FL1-H	No Gate
---	052199.007	FL1-H	No Gate

Fig  
7C

Key	Name	Parameter	Gate
—	052199.003	FL1-H	No Gate
---	052199.008	FL1-H	No Gate

Fig  
7D

Key	Name	Parameter	Gate
—	052199.004	FL1-H	No Gate
---	052199.009	FL1-H	No Gate

Fig  
7E

Key	Name	Parameter	Gate
—	052199.005	FL1-H	No Gate
---	052199.010	FL1-H	No Gate

Figure 7

Fig 8A

Jurkat CTLA4 NEGATIVE cell line

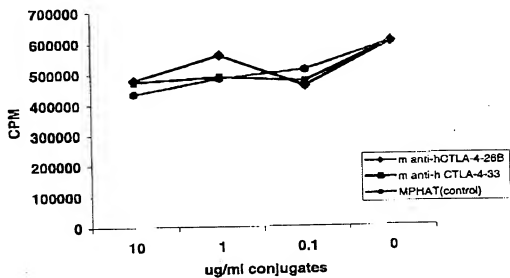
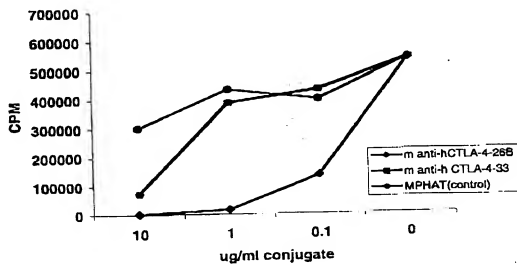


Fig 8B

Jurkat CTLA-4 POSITIVE cell line





HuCTLA4 - Vk

TATATCTAGACCACCATGGATTTTCAAGTGCAGATCTTCAGCTTCTCTGCTAATCAGTGCC  
M D F Q V Q I F S F L L I S A

TCAGTCATACTGTCCAGAGGAGATATCCAGATGACCCAGTCTCCATCCTCCCTATCCGCA  
S V I L S R G D I Q M T Q S P S S L S A

TCTGTGGGGACAGGGTCACCATAACCTGTAGTGCCACCTCAAGTATAACTTACATGTCC  
S V G D R V T I T C S A T S S I T Y M S

TGGTATCAGCAGAAGCCAGGAAAGGCTCCCAAGCTTCTGATTTATGACACATCCAACCTG  
W Y Q Q K P G K A P K L L I Y D T S N L

GCTTCTGGGGTACCTAGCCGCTTCAGTGGCAGTGGGTCTGGGACCGACTACACACTCACA  
A S G V P S R F S G S G S G T D Y T L T

ATCAGCAGCCTGCAGCCAGAAGATTTTGCCACTTATTACTGCCAGCAGTGGAGTAGTTAC  
I S S L Q P E D F A T Y Y C Q Q W S S Y

CCGCTCACGTTTCGGTGGAGGGACCAAGGTTGAGATAAAACGTAAGTAGAATCCAAAGTCT  
P L T F G G G T K V E I K

AGATATA

Figure 9

00772103-04301

HuCTLA4 - VH

TATATCTAGACCACCATGGCTGTCTCTGGTGTCTTCTCTGCCTGGTGCATTTCCAAGC  
M A V L V L F L C L V A F P S

TGTGTCTCTGTCCCAGGTGCAGCTGCAAGAGTCAGGACCTGGCCTGGTGAAGCCCTCACAG  
C V L S Q V Q L Q E S G P G L V K P S Q

ACACTGTCCTTGACTTGCACTGTCTCTGGGTTTTTATTAACTCATATGGTGTATATTGG  
T L S L T C T V S G F S L T S Y G V Y W

GTTCGCCAGCCTCCAGGAAAGGCTCTGGAGTGGCTGGGAGTAATATGGGCTGGTGGTACC  
V R Q P G K G L E W L G V I W A G G T

ACAAATTATAATTTCGGCTCTCATGTCCAGACTGACAATCAGCAAAGACACATCCAAGAAC  
T N Y N S A L M S R L T I S K D T S K N

CAAGTTTCCTTAAACTCAGCAGTGTGACTGCAGCGGACACAGCCGTCTACTACTGTGCC  
Q V S L K L S S V T A A D T A V Y Y C A

CGAGGCCCCCGCACGCTATGATGAAGAGAGGCTATGCTATGGACTACTGGGGACAAGGA  
R G P P H A M M K R G Y A M D Y W G Q G

ACCCTAGTCACAGTCTCTCTCAGGTGAGTCCTTAAACCTCTAGATATA  
T L V T V S S

077210-2301  
10826-22270

Figure 10

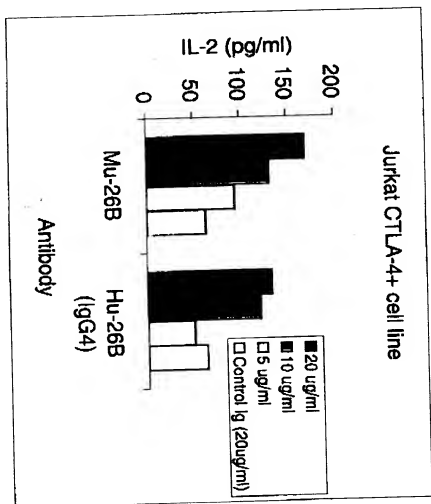


Figure 11

09772403-012604